

On page 10, beginning on line 1, please replace the paragraph beginning, "Fig. 7" with the following paragraph:

96 Figs. 7A-7D show diagrammatically the enhanced expression of activation molecules on T lymphocytes after costimulation by 8F4. Open circles (○) represent 8F4 antibodies; triangles (◆) represent nonspecific antibodies of the same isotype; filled circles (●) represent anti-CD28 antibodies-9.3.

On page 24, please insert the following new paragraph at line 26 (*i.e.*, after the priority paragraph):

#### DEPOSIT OF HYBRIDOMA

97 The hybridoma 8F4, secreting native monoclonal antibody 8F4, was deposited with the Deutsche Sammlung Von Mikroorganismen und ZellKulturen GmbH ("DSMZ"), at Mascheroder Weg 1b, D-3300 Braunschweig, Germany, on April 9, 2002, in compliance with the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure on behalf of the Applicant and the Robert-Koch-Institut. The deposited hybridoma was assigned DSMZ accession number DSM ACC2539.

#### IN THE CLAIMS:

Please amend the claims as follows:

Amend claims 71, 76, 78, 83, 85, 86 and 88 and 97 to read as follows:

71. (Three times amended) A monoclonal antibody that recognizes a human 8F4 polypeptide, wherein said 8F4 polypeptide:

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- a) is an inducible T cell costimulatory molecule;
  - b) occurs on two-signal-activated human T lymphocytes;
  - c) exhibits a molecular weight of about 55 to 60 kilodaltons as determined by non-reducing sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE); and
  - d) is a dimer of two peptide chains exhibiting molecular weights of about 27 kilodaltons and 29 kilodaltons, as measured by reducing SDS-PAGE,

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wherein the human 8F4 polypeptide is recognized by the antibody deposited with the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH ("DSMZ") and assigned accession no. DSM ACC2539;

and wherein the monoclonal antibody, in conjunction with anti-CD3 monoclonal antibody OKT3, costimulates proliferation of human T lymphocytes.

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76. (Three times amended) A monoclonal antibody that recognizes a human 8F4 polypeptide, wherein said 8F4 polypeptide:

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- a) is an inducible T cell costimulatory molecule;
  - b) occurs on two-signal-activated human T lymphocytes;
  - c) exhibits a molecular weight of about 55 to 60 kilodaltons as determined by non-reducing sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE); and
  - d) is a dimer of two peptide chains exhibiting molecular weights of about 27 kilodaltons and 29 kilodaltons, as measured by reducing SDS-PAGE,

wherein the human 8F4 polypeptide is recognized by the antibody deposited with the DSMZ and assigned accession no. DSM ACC2539;

wherein the monoclonal antibody, when immobilized on a solid surface and in conjunction with anti-CD3 monoclonal antibody OKT3, costimulates proliferation of human T lymphocytes;

and wherein the monoclonal antibody inhibits costimulation of T lymphocytes by the human 8F4 polypeptide.

78. (Three times amended) A hybridoma that produces a monoclonal antibody that recognizes a human 8F4 polypeptide, wherein said 8F4 polypeptide:

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- a) is an inducible T cell costimulatory molecule;
  - b) occurs on two-signal-activated human T lymphocytes;
  - c) exhibits a molecular weight of about 55 to 60 kilodaltons as determined by non-reducing sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE); and

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d) is a dimer of two peptide chains exhibiting molecular weights of about 27 kilodaltons and 29 kilodaltons, as measured by reducing SDS-PAGE, wherein the human 8F4 polypeptide is recognized by the antibody deposited with the DSMZ and assigned accession no. DSM ACC2539; and wherein the hybridoma produces a monoclonal antibody that, in conjunction with anti-CD3 monoclonal antibody OKT3, costimulates proliferation of human T lymphocytes.

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83. (Three times amended) A hybridoma that produces a monoclonal antibody that recognizes a human 8F4 polypeptide, wherein said 8F4 polypeptide:

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a) is an inducible T cell costimulatory molecule;

b) occurs on two-signal-activated human T lymphocytes;

c) exhibits a molecular weight of about 55 to 60 kilodaltons as determined by non-reducing sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE), and

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d) is a dimer of two peptide chains exhibiting molecular weights of about 27 kilodaltons and 29 kilodaltons, as measured by reducing SDS-PAGE, wherein the human 8F4 polypeptide is recognized by the antibody deposited with the DSMZ and assigned accession no. DSM ACC2539; wherein hybridoma produces a monoclonal antibody, wherein the monoclonal antibody, when immobilized on a solid surface and in conjunction with anti-CD3 monoclonal antibody OKT3, costimulates proliferation of human T lymphocytes; and wherein the monoclonal antibody inhibits costimulation of T lymphocytes by the human 8F4 polypeptide.

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85. (Three times amended) A pharmaceutical composition comprising a monoclonal antibody that recognizes a human 8F4 polypeptide, wherein said 8F4 polypeptide:

- a) is an inducible T cell costimulatory molecule;
- b) occurs on two-signal-activated human T lymphocytes;

c) exhibits a molecular weight of about 55 to 60 kilodaltons as determined by non-reducing sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE); and

d) is a dimer of two peptide chains exhibiting molecular weights of about 27 kilodaltons and 29 kilodaltons, as measured by reducing SDS-PAGE,

wherein the human 8F4 polypeptide is recognized by the antibody deposited with the DSMZ and assigned accession no. DSM ACC2539;

and wherein the pharmaceutical composition comprises a monoclonal antibody that, in conjunction with anti-CD3 monoclonal antibody OKT3, costimulates proliferation of human T lymphocytes.

86. (Three times amended) A pharmaceutical composition comprising a monoclonal antibody that recognizes a human 8F4 polypeptide, wherein said 8F4 polypeptide:

a) is an inducible T cell costimulatory molecule;

b) occurs on two-signal-activated human T lymphocytes;

c) exhibits a molecular weight of about 55 to 60 kilodaltons as determined by non-reducing sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE); and

d) is a dimer of two peptide chains exhibiting molecular weights of about 27 kilodaltons and 29 kilodaltons, as measured by reducing SDS-PAGE,

wherein the human 8F4 polypeptide is recognized by the antibody deposited with the DSMZ and assigned accession no. DSM ACC2539;

and wherein the pharmaceutical composition comprises a monoclonal antibody;

wherein the monoclonal antibody, when immobilized on a solid surface and in conjunction with anti-CD3 monoclonal antibody OKT3, costimulates proliferation of human T lymphocytes;

and wherein the monoclonal antibody inhibits costimulation of T lymphocytes by the human 8F4 polypeptide.

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88. (Amended) A method for producing the monoclonal antibody of claim 71 or 76, comprising: culturing an antibody-secreting hybridoma obtained by:

- (i) fusion of a myeloma cell line cell with a spleen cell of a mouse immunized with 2-signal-activated human T lymphocytes; and
- (ii) selection of a hybridoma that produces said antibody, such that the monoclonal antibody is produced.

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97. (Three times amended) A method of producing a human 8F4 polypeptide-specific monoclonal antibody, comprising: culturing an antibody-secreting hybridoma obtained by (i) fusion of a myeloma cell line cell with a spleen cell of a mouse immunized with an antigen comprising a human 8F4 polypeptide and (ii) selection of a hybridoma that produces said antibody, wherein said human 8F4 polypeptide:

- a) is an inducible T cell costimulatory molecule;
- b) occurs on two-signal-activated human T lymphocytes;
- c) exhibits a molecular weight of about 55 to 60 kilodaltons as determined by non-reducing sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE); and
- d) is a dimer of two peptide chains exhibiting molecular weights of about 27 kilodaltons and 29 kilodaltons, as measured by reducing SDS-PAGE,

and wherein the human 8F4 polypeptide is recognized by the antibody deposited with the DSMZ and assigned accession no. DSM ACC2539; such that the monoclonal antibody is produced.

Please add the following new claims:

101. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced T lymphocyte proliferation.

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102. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced ATAC expression.

103. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced CD25 expression.

104. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced CD69 expression.

105. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced TRAP expression.

916 106. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of T lymphocyte induction of immunoglobulin production by B lymphocytes.

107. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced reduction of apoptosis in activated T lymphocytes.

108. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced T lymphocyte proliferation.

109. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced ATAC expression.

110. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced CD25 expression.

111. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced CD69 expression.

112. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced TRAP expression.

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113. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of T lymphocyte induction of immunoglobulin production by B lymphocytes.

114. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced reduction of apoptosis in activated T lymphocytes.

115. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced T lymphocyte proliferation.

116. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced ATAC expression.

117. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced CD25 expression.

118. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced CD69 expression.

119. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced TRAP expression.

120. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of T lymphocyte induction of immunoglobulin production by B lymphocytes.

916 121. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of 8F4-induced reduction of apoptosis in activated T lymphocytes.

122. (New) The monoclonal antibody of claim 76, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of: 8F4-induced T lymphocyte proliferation, 8F4-induced ATAC expression, 8F4-induced CD25 expression, 8F4-induced CD69 expression, 8F4-induced TRAP expression, T lymphocyte induction of immunoglobulin production by B lymphocytes and 8F4-induced reduction of apoptosis in activated T lymphocytes.

123. (New) The hybridoma of claim 83, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of: 8F4-induced T lymphocyte proliferation, 8F4-induced ATAC expression, 8F4-induced CD25 expression, 8F4-induced CD69 expression, 8F4-induced TRAP expression, T lymphocyte induction of immunoglobulin production by B lymphocytes and 8F4-induced reduction of apoptosis in activated T lymphocytes.



124. (New) The pharmaceutical composition of claim 86, wherein the monoclonal antibody inhibition of costimulation of T lymphocytes by the human 8F4 polypeptide is exhibited as an inhibition of: 8F4-induced T lymphocyte proliferation, 8F4-induced ATAC expression, 8F4-induced CD25 expression, 8F4-induced CD69 expression, 8F4-induced TRAP expression, T lymphocyte induction of immunoglobulin production by B lymphocytes and 8F4-induced reduction of apoptosis in activated T lymphocytes.

125. (New) The monoclonal antibody of claim 71, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:10,000.

126. (New) The monoclonal antibody of claim 71, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:5,000.

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127. (New) The monoclonal antibody of claim 71, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:2,500.

128. (New) The monoclonal antibody of claim 71, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:1,000.

129. (New) The monoclonal antibody of claim 76, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:10,000.

130. (New) The monoclonal antibody of claim 76, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:5,000.

131. (New) The monoclonal antibody of claim 76, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:2,500.

132. (New) The monoclonal antibody of claim 76, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:1,000.

133. (New) The hybridoma of claim 78, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:10,000.

134. (New) The hybridoma of claim 78, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:5,000.

135. (New) The hybridoma of claim 78, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:2,500.

136. (New) The hybridoma of claim 78, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:1,000.

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137. (New) The hybridoma of claim 83, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:10,000.

138. (New) The hybridoma of claim 83, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:5,000.

139. (New) The hybridoma of claim 83, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:2,500.

140. (New) The hybridoma of claim 83, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:1,000.

141. (New) The pharmaceutical composition of claim 85, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:10,000.

142. (New) The pharmaceutical composition of claim 85, wherein the costimulation of proliferation of human T lymphocytes is exhibited at a dilution of OKT-3 of 1:5,000.